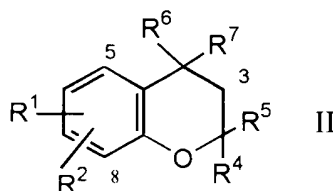


4. A compound of the formula:



wherein

R<sup>1</sup> is OH, O(CH<sub>2</sub>)<sub>1-2</sub>OH, OCH<sub>2</sub>CO<sub>2</sub>H, CO<sub>2</sub>H, O-Z-C(O)NH(CH<sub>2</sub>)<sub>1-6</sub>R<sup>17</sup> or  
OCH<sub>2</sub>-4-Phe-C(O)NH(CH<sub>2</sub>)<sub>1-6</sub>R<sup>17</sup>;

R<sup>2</sup> is H or lower alkyl;

R<sup>3</sup> is H, alkyl, aryl, or arylalkyl;

R<sup>4</sup> and R<sup>5</sup> are each independently H, lower alkyl, or substituted lower alkyl where the  
substituents are 1-3 alkoxy, aryl, substituted aryl, carboalkoxy, carboxamido or  
di-loweralkylamido; or

R<sup>4</sup> and R<sup>5</sup> taken together are -(CH<sub>2</sub>)<sub>n</sub>-, -(CH<sub>2</sub>)<sub>2</sub>-O-(CH<sub>2</sub>)<sub>2</sub>-, -CH<sub>2</sub>-O-(CH<sub>2</sub>)<sub>3</sub>-, -(CH<sub>2</sub>)<sub>2</sub>-NR<sup>8</sup>-CH<sub>2</sub>)<sub>2</sub>-,  
-CH<sub>2</sub>-NR<sup>8</sup>-(CH<sub>2</sub>)<sub>m</sub>-, -(CH<sub>2</sub>)<sub>2</sub>CH(NHR<sup>8</sup>)(CH<sub>2</sub>)<sub>2</sub>-, -(CH<sub>2</sub>)<sub>2</sub>-S(O)<sub>0-2</sub>-(CH<sub>2</sub>)<sub>2</sub>-, or  
-CH<sub>2</sub>CH(N-loweralkyl)(CH<sub>2</sub>)<sub>2</sub>CHCH<sub>2</sub>-;

one of R<sup>6</sup> and R<sup>7</sup> is H and the other is H, OH, or N(CH<sub>2</sub>)<sub>1-6</sub>R<sup>14</sup>R<sup>15</sup>; or

R<sup>6</sup> and R<sup>7</sup> taken together are or with the proviso that

when R<sup>1</sup> is -OH and R<sup>2</sup> is -H, R<sup>6</sup> and R<sup>7</sup> are not -H and -OH or when taken together are

not ;

R<sup>8</sup> is H, COOR<sup>9</sup>, CONHR<sup>10</sup>, CSNHR<sup>11</sup>, COR<sup>12</sup>, SO<sub>2</sub>R<sup>13</sup>, lower alkyl, aryl lower alkyl,  
heteroaryl, or heteroaryl lower alkyl, wherein aryl is optionally substituted with 1-3  
substituents selected from lower alkyl, lower alkoxy, halo, CN, NH<sub>2</sub>, COOH, CONH<sub>2</sub>,

carboalkoxy, and mono- or di-lower alkylamino and wherein heteroaryl is a mono- or bicyclic heteroaromatic ring system of 5 to 10 members including 1 to 3 heteroatoms selected from O, N, and S and 0-3 substituents selected from halo, amino, cyano, lower alkyl, carboalkoxy, CONH<sub>2</sub>, and S-lower alkyl;

R<sup>9</sup> is lower alkyl, aryl, aryl lower alkyl, heteroaryl, aryl substituted by 1-3 substituents selected from alkyl, alkenyl, alkoxy, methylene dioxy, and halo, or a 5- to 6-membered heterocyclic ring containing O or N as a heteroatom, wherein heteroaryl is a heteroaromatic ring of 5 to 6 members including 1 to 2 heteroatoms selected from O, N, and S and 0-2 substituents selected from lower alkyl, dialkylamino, lower alkoxy, and halo;

R<sup>10</sup> and R<sup>11</sup> are each independently lower alkyl, aryl, aryl lower alkyl, or aryl substituted by 1-3 substituents selected from lower alkyl, halo, alkoxy and haloalkyl;

R<sup>12</sup> is lower alkyl, aryl, heteroaryl, aryl lower alkyl, heteroaryl lower alkyl, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from O, S, and N, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from O, S, and N-lower alkyl, or aryl substituted with 1-3 substituents selected from lower alkyl, alkoxy, halo, sulfamoyl, lower alkyl sulfamoyl, cyano, and phenyl;

R<sup>13</sup> is lower alkyl, aryl, or aryl substituted with 1-3 substituents selected from lower alkyl, alkoxy, halo, CN, and haloalkyl;

R<sup>14</sup> is H, alkyl; alkyl substituted by 1-3 alkoxy, S-lower alkyl, sulfamoyl, halo, alkylsulphonamido, or arylsulphonamido; alkenyl; alkynyl; aryl; substituted aryl; heteroaryl; substituted heteroaryl; heterocycloalkyl; -CH<sub>2</sub>NR<sup>16</sup>C(O)R<sup>16</sup>; -C(O)NR<sup>16</sup>R<sup>16</sup>; -CH<sub>2</sub>OC(O)R<sup>16</sup>; or -CH<sub>2</sub>SC(O)R<sup>16</sup>;

R<sup>15</sup> is H, alkyl, -C(O)X, -C(S)X, or -C(NCN)NR<sup>3</sup>R<sup>3</sup>;

R<sup>16</sup> is lower alkyl, substituted lower alkyl, aryl, or substituted aryl;

R<sup>17</sup> is H, alkyl; alkyl substituted by 1-3 alkoxy, S-lower alkyl, sulfamoyl, halo, alkylsulphonamido, or arylsulphonamido; alkenyl; alkynyl; aryl; substituted aryl;

heteroaryl; substituted heteroaryl; heterocycloalkyl;  $-\text{CH}_2\text{NR}^{16}\text{C}(\text{O})\text{R}^{16}$ ,  $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{16}$ ,  
 $-\text{CH}_2\text{OC}(\text{O})\text{R}^{16}$ ; or  $-\text{CH}_2\text{SC}(\text{O})\text{R}^{16}$ ;

X is alkyl, aryl, arylalkyl, O-loweralkyl, or  $-\text{NR}^3\text{R}^3$ ;

Z is  $-(\text{CH}_2)_{1-6}-$ , optionally substituted with 1-3 lower alkyl;  $-\text{CHR}^2-$ ;  $-\text{Phe}-\text{CH}_2-$ , where Phe is  
 optionally mono-substituted with halogen, lower alkyl, or alkoxy; or heteroarylene- $(\text{CH}_2)-$ ;

m is 2 or 3; and

n is 4-9;

or a pharmaceutically acceptable salt thereof.

5. A compound of claim 4, wherein  $\text{R}^{12}$  is sulfamoylphenyl.

6. A compound of claim 4, wherein  $\text{R}^{12}$  is p-sulfamoylphenyl.

7. A compound of claim 4, wherein:

$\text{R}^1$  is OH,  $\text{OCH}_2\text{C}(\text{O})\text{NH}(\text{CH}_2)_{1-6}\text{R}^{17}$ , or  $\text{OCH}_2-4\text{-Phe}-\text{C}(\text{O})\text{NH}(\text{CH}_2)_{1-6}\text{R}^{17}$ ;

$\text{R}^4$  and  $\text{R}^5$  are each lower alkyl; or

$\text{R}^4$  and  $\text{R}^5$  taken together are  $-(\text{CH}_2)_5-$ ,  $-(\text{CH}_2)_2\text{-O-}(\text{CH}_2)_2-$ ,  $-(\text{CH}_2)_2\text{-NR}^8\text{-(CH}_2)_2-$ ,  
 $-(\text{CH}_2)_2\text{-CH(NHR}^8\text{)(CH}_2)_2-$ ,  $-(\text{CH}_2)_2\text{-S-(CH}_2)_2-$ , or  $-\text{CH}_2\text{CH}(\text{NCH}_3)(\text{CH}_2)_2\text{CHCH}_2-$ ;

$\text{R}^6/\text{R}^7$  are H/OH or  $-\text{S}(\text{CH}_2)_2\text{S-}$ ;

$\text{R}^8$  is H,  $\text{COOR}^9$ ,  $\text{CONHR}^{10}$ ,  $\text{CSNHR}^{11}$ ,  $\text{COR}^{12}$ ,  $\text{SO}_2\text{R}^{13}$ , lower alkyl, aryl lower alkyl,  
 heteroaryl wherein the heteroatoms include 1 to 3 N atoms and the substituents are halo or  
 amino, heteroaryl lower alkyl wherein heteroaryl is 6-membered and the heteroatoms are  
 N, or aryl lower alkyl substituted with 1 substituent selected from lower alkyl, alkoxy, and  
 halo;

$\text{R}^9$  is lower alkyl, aryl lower alkyl, aryl, tetrahydrofuranyl, tetrahydropyranyl, or aryl  
 substituted by 1 to 2 substituents selected from lower alkyl, alkenyl, alkoxy, methylene  
 dioxy, and halo;

$R^{10}$  and  $R^{11}$  are each independently aryl, aryl lower alkyl, or aryl substituted by 1 substituent selected from lower alkyl, halo, alkoxy, trifluoromethyl, and pentafluoroethyl;

$R^{12}$  is lower alkyl, aryl, aryl lower alkyl, heteroaryl lower alkyl wherein the heteroatoms are N, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from S and N lower alkyl, or aryl substituted with 1 substituent selected from lower alkyl, alkoxy, halo, sulfamoyl, cyano, or phenyl; and

$R^{13}$  is lower alkyl, aryl, or aryl substituted with 1 substituent selected from lower alkyl, alkoxy, and halo;

or a pharmaceutically acceptable salt thereof.

38. A compound of claim 4 wherein:

$R^1$  is  $\text{OCH}_2\text{CO}_2\text{H}$ ;

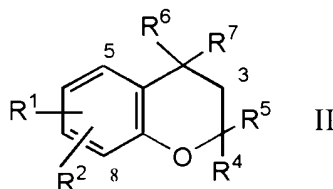
$R^2$  is  $-\text{H}$ ;

$R^4$  and  $R^5$  taken together are  $-(\text{CH}_2)_2-\text{S}-(\text{O})_2-(\text{CH}_2)_2-$ ; and

one of  $R^6$  and  $R^7$  is  $-\text{H}$  and the other is  $-\text{N}(\text{CH}_2)_{1-6}\text{R}^{14}\text{R}^{15}$ .

The foregoing amended claims effect the following changes:

4. (thrice amended) A compound of the formula:



wherein:

$R^1$  is  $\text{OH}$ ,  $\text{O}(\text{CH}_2)_{1-2}\text{OH}$ ,  $\text{OCH}_2\text{CO}_2\text{H}$ ,  $\text{CO}_2\text{H}$ ,  $\text{O}-\text{Z}-\text{C}(\text{O})\text{NH}(\text{CH}_2)_{1-6}\text{R}^{17}$  or  $\text{OCH}_2-4\text{-Phe}-\text{C}(\text{O})\text{NH}(\text{CH}_2)_{1-6}\text{R}^{17}$ ;


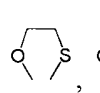



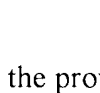
$R^2$  is H or lower alkyl;

$R^3$  is H, alkyl, aryl, or arylalkyl;


$R^4$  and  $R^5$  are each independently H, lower alkyl, or substituted lower alkyl where the substituents are 1-3 alkoxy, aryl, substituted aryl, carboalkoxy, carboxamido or di-loweralkylamido; or

$R^4$  and  $R^5$  taken together are  $-(CH_2)_n-$ ,  $-(CH_2)_2-O-(CH_2)_2-$ ,  $-CH_2-O-(CH_2)_3-$ ,  $-(CH_2)_2-NR^8-(CH_2)_2-$ ,  $-CH_2-NR^8-(CH_2)_m-$ ,  $-(CH_2)_2CH(NHR^8)(CH_2)_2-$ ,  $-(CH_2)_2-S(O)_{0-2}-(CH_2)_2-$ , or  $-CH_2CH(N-\text{loweralkyl})(CH_2)_2CHCH_2-$ ;

one of  $R^6$  and  $R^7$  is H and the other is H, OH, or  $N(CH_2)_{1-6}R^{14}R^{15}$ , or

$R^6$  and  $R^7$  taken together are  $\left[ \begin{array}{c} \text{O} \\ \parallel \\ \text{---} \end{array} \right]$ , , , , , or  or , with the proviso that

when  $R^1$  is -OH and  $R^2$  is -H,  $R^6$  and  $R^7$  are not -H and -OH or when taken together are

not ;

$R^8$  is H,  $COOR^9$ ,  $CONHR^{10}$ ,  $CSNHR^{11}$ ,  $COR^{12}$ ,  $SO_2R^{13}$ , lower alkyl, aryl lower alkyl, heteroaryl, or heteroaryl lower alkyl, wherein aryl is optionally substituted with 1-3 substituents selected from lower alkyl, lower alkoxy, halo, CN,  $NH_2$ ,  $COOH$ ,  $CONH_2$ , carboalkoxy, and mono- or di-lower alkylamino and wherein heteroaryl is a mono- or bicyclic heteroaromatic ring system of 5 to 10 members including 1 to 3 heteroatoms selected from O, N, and S and 0-3 substituents selected from halo, amino, cyano, lower alkyl, carboalkoxy,  $CONH_2$ , and S-lower alkyl;

$R^9$  is lower alkyl, aryl, aryl lower alkyl, heteroaryl, aryl substituted by 1-3 substituents selected from alkyl, alkenyl, alkoxy, methylene dioxy, and halo, or a 5- to 6-membered heterocyclic ring [wherein the hetero atom is] **containing** O or N **as a heteroatom**, wherein

heteroaryl is a heteroaromatic ring of 5 to 6 members including 1 to 2 heteroatoms selected from O, N, and S and 0-2 substituents selected from lower alkyl, dialkylamino, lower alkoxy, and halo;

R<sup>10</sup> and R<sup>11</sup> are each independently lower alkyl, aryl, aryl lower alkyl, or aryl substituted by 1-3 substituents selected from lower alkyl, halo, alkoxy and haloalkyl;

R<sup>12</sup> is lower alkyl, aryl, heteroaryl, aryl lower alkyl, heteroaryl lower alkyl, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from O, S, and N, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from O, S, and N-lower alkyl, or aryl substituted with 1-3 substituents selected from lower alkyl, alkoxy, halo, sulfamoyl, lower alkyl sulfamoyl, cyano, and phenyl;

R<sup>13</sup> is lower alkyl, aryl, or aryl substituted with 1-3 substituents selected from lower alkyl, alkoxy, halo, CN, and haloalkyl;

R<sup>14</sup> is H; alkyl; alkyl substituted by 1-3 alkoxy, S-lower alkyl, sulfamoyl, halo, alkylsulphonamido, or arylsulphonamido; alkenyl; alkynyl; aryl; substituted aryl; heteroaryl; substituted heteroaryl; heterocycloalkyl; -CH<sub>2</sub>NR<sup>16</sup>C(O)R<sup>16</sup>, -C(O)NR<sup>16</sup>R<sup>16</sup>, -CH<sub>2</sub>OC(O)R<sup>16</sup>; or -CH<sub>2</sub>SC(O)R<sup>16</sup>;

R<sup>15</sup> is H, alkyl, -C(O)X, -C(S)X, or -C(NCN)NR<sup>3</sup>R<sup>3</sup>;

R<sup>16</sup> is lower alkyl, substituted lower alkyl, aryl, or substituted aryl;

R<sup>17</sup> is H; alkyl; alkyl substituted by 1-3 alkoxy, S-lower alkyl, sulfamoyl, halo, alkylsulphonamido, or arylsulphonamido; alkenyl; alkynyl; aryl; substituted aryl; heteroaryl; substituted heteroaryl; heterocycloalkyl; -CH<sub>2</sub>NR<sup>16</sup>C(O)R<sup>16</sup>, -C(O)NR<sup>16</sup>R<sup>16</sup>, -CH<sub>2</sub>OC(O)R<sup>16</sup>; or -CH<sub>2</sub>SC(O)R<sup>16</sup>;

X is alkyl, aryl, arylalkyl, O-loweralkyl, or -NR<sup>3</sup>R<sup>3</sup>;

Z is -(CH<sub>2</sub>)<sub>1-6</sub>-, optionally substituted with 1-3 lower alkyl; -CHR<sup>2</sup>-; -Phe-CH<sub>2</sub>-, where Phe is optionally mono-substituted with halogen, lower alkyl, or alkoxy; or heteroarylene-(CH<sub>2</sub>)<sub>n</sub>;

m is 2 or 3; **and**

n is 4-9;

or a pharmaceutically acceptable salt thereof.

5. (once amended) A compound of claim 4    wherein R<sup>12</sup> is sulfamoylphenyl.

6. (once amended) A compound of claim 4    wherein R<sup>12</sup> is *p*-sulfamoylphenyl.

7. (once amended) A compound of claim 4    wherein:

R<sup>1</sup> is OH, OCH<sub>2</sub>C(O)NH(CH<sub>2</sub>)<sub>1-6</sub>R<sup>17</sup>, or OCH<sub>2</sub>-4-Phe-C(O)NH(CH<sub>2</sub>)<sub>1-6</sub>R<sup>17</sup>;

R<sup>4</sup> and R<sup>5</sup> are each lower alkyl; or

R<sup>4</sup> and R<sup>5</sup> taken together are -(CH<sub>2</sub>)<sub>5</sub>-, -(CH<sub>2</sub>)<sub>2</sub>-O-(CH<sub>2</sub>)<sub>2</sub>-, -(CH<sub>2</sub>)<sub>2</sub>-NR<sup>8</sup>-(CH<sub>2</sub>)<sub>2</sub>-,  
 -(CH<sub>2</sub>)<sub>2</sub>-CH(NHR<sup>8</sup>)(CH<sub>2</sub>)<sub>2</sub>-, -(CH<sub>2</sub>)<sub>2</sub>-S-(CH<sub>2</sub>)<sub>2</sub>-, or -CH<sub>2</sub>CH(NCH<sub>3</sub>)(CH<sub>2</sub>)<sub>2</sub>CHCH<sub>2</sub>- ;

R<sup>6</sup>/R<sup>7</sup> are H/OH [ ; =O , ] or -S(CH<sub>2</sub>)<sub>2</sub>S-;

R<sup>8</sup> is H, COOR<sup>9</sup>, CONHR<sup>10</sup>, CSNHR<sup>11</sup>, COR<sup>12</sup>, SO<sub>2</sub>R<sup>13</sup>, lower alkyl, aryl lower alkyl, heteroaryl wherein the [ ring members ] **heteroatoms** include 1 to 3 N atoms and the substituents are halo or amino, heteroaryl lower alkyl wherein heteroaryl is 6-membered and the heteroatoms are N, or aryl lower alkyl substituted with 1 substituent selected from lower alkyl, alkoxy, and halo;

R<sup>9</sup> is lower alkyl, aryl lower alkyl, aryl, tetrahydrofuranyl, tetrahydropyranyl, or aryl substituted by 1 to 2 substituents selected from lower alkyl, alkenyl, alkoxy, methylene dioxy, and halo;

R<sup>10</sup> and R<sup>11</sup> are each independently aryl, aryl lower alkyl, or aryl substituted by 1 substituent selected from lower alkyl, halo, alkoxy, trifluoromethyl, and pentafluoroethyl;

R<sup>12</sup> is lower alkyl, aryl, aryl lower alkyl, heteroaryl lower alkyl wherein the heteroatoms are N, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from S and N

lower alkyl, or aryl substituted with 1 substituent selected from lower alkyl, alkoxy, halo, sulfamoyl, cyano, or phenyl; **and**

R<sup>13</sup> is lower alkyl, aryl, or aryl substituted with 1 substituent selected from lower alkyl, alkoxy, and halo;

or a pharmaceutically acceptable salt thereof.

38. (once amended) A compound of claim 4 wherein:

R<sup>1</sup> is OCH<sub>2</sub>CO<sub>2</sub>H;

R<sup>2</sup> is -H,

R<sup>4</sup> and R<sup>5</sup> taken together are -(CH<sub>2</sub>)<sub>2</sub>-S-(O)<sub>2</sub>-(CH<sub>2</sub>)<sub>2</sub>-; **and**

one of R<sup>6</sup> and R<sup>7</sup> is -H and the other is -H or -N(CH<sub>2</sub>)<sub>1-6</sub>R<sup>14</sup>R<sup>15</sup> [ ;

R<sup>14</sup> is -H, and

R<sup>15</sup> is alkyl ] .

### III. New Claims

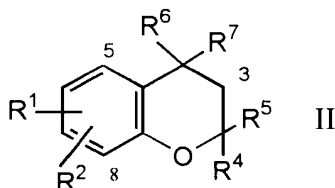
Please add new claims 39-49.

39. A compound of claim 38 wherein:

R<sup>14</sup> is -H, and

R<sup>15</sup> is alkyl.

40. A compound of the formula:





wherein:

$R^1$  is  $OCH_2CO_2H$ ;

$R^2$  is H;

$R^4$  and  $R^5$  taken together are  $-(CH_2)_2-S-(O)_2-(CH_2)_2-$ ; and

one of  $R^6$  and  $R^7$  is -H and the other is -H or  $-N(CH_2)_{1-6}R^{14}R^{15}$ ,

wherein:

$R^{14}$  is H; alkyl; alkyl substituted by 1-3 alkoxy, S-lower alkyl, sulfamoyl, halo, alkylsulphonamido, or arylsulphonamido; alkenyl; alkynyl; aryl; substituted aryl; heteroaryl; substituted heteroaryl; heterocycloalkyl;  $-CH_2NR^{16}C(O)R^{16}$ ;  $-C(O)NR^{16}R^{16}$ ;  $-CH_2OC(O)R^{16}$ ; or  $-CH_2SC(O)R^{16}$ ;

wherein:

$R^{16}$  is lower alkyl, substituted lower alkyl, aryl, or substituted aryl; and

$R^{15}$  is H, alkyl,  $-C(O)X$ ,  $-C(S)X$ , or  $-C(NCN)NR^3R^3$ ;

wherein:

X is alkyl, aryl, arylalkyl, O-loweralkyl, or  $-NR^3R^3$ ; and

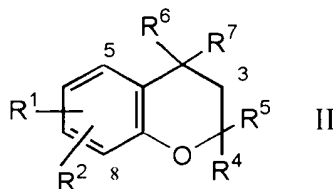
$R^3$  is H, alkyl, aryl, or arylalkyl.

41. A compound of claim 40, wherein:

$R^{14}$  is -H; and

$R^{15}$  is alkyl.

42. A compound of the formula:



wherein:

$R^1$  is OH,  $O(CH_2)_{1-2}OH$ ,  $OCH_2CO_2H$ ,  $CO_2H$ ,  $O-Z-C(O)NH(CH_2)_{1-6}R^{17}$  or  $OCH_2-4-Phe-C(O)NH(CH_2)_{1-6}R^{17}$ ;

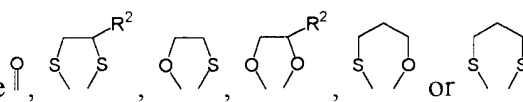
$R^2$  is H or lower alkyl;

$R^3$  is H, alkyl, aryl, or arylalkyl;

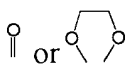
$R^4$  and  $R^5$  are each independently H, lower alkyl, or substituted lower alkyl where the substituents are 1-3 alkoxy, aryl, substituted aryl, carboalkoxy, carboxamido or di-loweralkylamido; or


$R^4$  and  $R^5$  taken together are  $-(CH_2)_n-$ ,  $-(CH_2)_2-O-(CH_2)_2-$ ,  $-CH_2-O-(CH_2)_3-$ ,  $-(CH_2)_2-NR^8-CH_2-$ ,  $-CH_2-NR^8-(CH_2)_m-$ ,  $-(CH_2)_2CH(NHR^8)(CH_2)_2-$ ,  $-(CH_2)_2-S(O)_{0-2}-(CH_2)_2-$ , or  $-CH_2CH(N-\text{loweralkyl})(CH_2)_2CHCH_2-$ ;

one of  $R^6$  and  $R^7$  is H and the other is H, OH, or  $N(CH_2)_{1-6}R^{14}R^{15}$ ; or

$R^6$  and  $R^7$  taken together are , with the proviso that

when  $R^1$  is -OH and  $R^2$  is -H,  $R^6$  and  $R^7$  are not -H and -OH or when taken together are

not  and when  $R^1$  is  $-OCH_2CO_2H$  and  $R^4$  and  $R^5$  are both -H or methyl,  $R^6$  and  $R^7$

taken together is not ;

$R^8$  is H,  $COOR^9$ ,  $CONHR^{10}$ ,  $CSNHR^{11}$ ,  $COR^{12}$ ,  $SO_2R^{13}$ , lower alkyl, aryl lower alkyl, heteroaryl, or heteroaryl lower alkyl, wherein aryl is optionally substituted with 1-3 substituents selected from lower alkyl, lower alkoxy, halo, CN,  $NH_2$ ,  $COOH$ ,  $CONH_2$ , carboalkoxy, and mono- or di-lower alkylamino and wherein heteroaryl is a mono- or bicyclic heteroaromatic ring system of 5 to 10 members including 1 to 3 heteroatoms selected from O, N, and S and 0-3 substituents selected from halo, amino, cyano, lower

alkyl, carboalkoxy, CONH<sub>2</sub>, and S-lower alkyl;

R<sup>9</sup> is lower alkyl, aryl, aryl lower alkyl, heteroaryl, aryl substituted by 1-3 substituents selected from alkyl, alkenyl, alkoxy, methylene dioxy, and halo, or a 5- to 6-membered heterocyclic ring containing O or N as a heteroatom, wherein heteroaryl is a heteroaromatic ring of 5 to 6 members including 1 to 2 heteroatoms selected from O, N, and S and 0-2 substituents selected from lower alkyl, dialkylamino, lower alkoxy, and halo;

R<sup>10</sup> and R<sup>11</sup> are each independently lower alkyl, aryl, aryl lower alkyl, or aryl substituted by 1-3 substituents selected from lower alkyl, halo, alkoxy and haloalkyl;

R<sup>12</sup> is lower alkyl, aryl, heteroaryl, aryl lower alkyl, heteroaryl lower alkyl, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from O, S, and N, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from O, S, and N-lower alkyl, or aryl substituted with 1-3 substituents selected from lower alkyl, alkoxy, halo, sulfamoyl, lower alkyl sulfamoyl, cyano, and phenyl;

R<sup>13</sup> is lower alkyl, aryl, or aryl substituted with 1-3 substituents selected from lower alkyl, alkoxy, halo, CN, and haloalkyl;

R<sup>14</sup> is H; alkyl; alkyl substituted by 1-3 alkoxy, S-lower alkyl, sulfamoyl, halo, alkylsulphonamido, or arylsulphonamido; alkenyl; alkynyl; aryl, substituted aryl; heteroaryl; substituted heteroaryl; heterocycloalkyl; -CH<sub>2</sub>NR<sup>16</sup>C(O)R<sup>16</sup>; -C(O)NR<sup>16</sup>R<sup>16</sup>; -CH<sub>2</sub>OC(O)R<sup>16</sup>; or -CH<sub>2</sub>SC(O)R<sup>16</sup>;

R<sup>15</sup> is H, alkyl, -C(O)X, -C(S)X, or -C(NCN)NR<sup>3</sup>R<sup>3</sup>;

R<sup>16</sup> is lower alkyl, substituted lower alkyl, aryl, or substituted aryl;

R<sup>17</sup> is H; alkyl, alkyl substituted by 1-3 alkoxy, S-lower alkyl, sulfamoyl, halo, alkylsulphonamido, or arylsulphonamido; alkenyl; alkynyl; aryl; substituted aryl; heteroaryl; substituted heteroaryl; heterocycloalkyl; -CH<sub>2</sub>NR<sup>16</sup>C(O)R<sup>16</sup>; -C(O)NR<sup>16</sup>R<sup>16</sup>; -CH<sub>2</sub>OC(O)R<sup>16</sup>; or -CH<sub>2</sub>SC(O)R<sup>16</sup>;

X is alkyl, aryl, arylalkyl, O-loweralkyl, or -NR<sup>3</sup>R<sup>3</sup>;

Z is -(CH<sub>2</sub>)<sub>1-6</sub>-, optionally substituted with 1-3 lower alkyl; -CHR<sup>2</sup>-; -Phe-CH<sub>2</sub>-, where Phe is

optionally mono-substituted with halogen, lower alkyl, or alkoxy; or heteroarylene-(CH<sub>2</sub>)-;  
 m is 2 or 3; and  
 n is 4-9;  
 or a pharmaceutically acceptable salt thereof.

43. A compound of claim 42, wherein R<sup>12</sup> is sulfamoylphenyl.

44. A compound of claim 42, wherein R<sup>12</sup> is *p*-sulfamoylphenyl.

45. A compound of claim 42, wherein:

R<sup>1</sup> is OH, OCH<sub>2</sub>C(O)NH(CH<sub>2</sub>)<sub>1-6</sub>R<sup>17</sup>, or OCH<sub>2</sub>-4-Phe-C(O)NH(CH<sub>2</sub>)<sub>1-6</sub>R<sup>17</sup>;

R<sup>4</sup> and R<sup>5</sup> are each lower alkyl; or

R<sup>4</sup> and R<sup>5</sup> taken together are -(CH<sub>2</sub>)<sub>5</sub>-, -(CH<sub>2</sub>)<sub>2</sub>-O-(CH<sub>2</sub>)<sub>2</sub>-, -(CH<sub>2</sub>)<sub>2</sub>-NR<sup>8</sup>-(CH<sub>2</sub>)<sub>2</sub>-,  
 -(CH<sub>2</sub>)<sub>2</sub>-CH(NHR<sup>8</sup>)(CH<sub>2</sub>)<sub>2</sub>-, -(CH<sub>2</sub>)<sub>2</sub>-S-(CH<sub>2</sub>)<sub>2</sub>-, or  $\text{-(CH}_2\text{)}_2\text{-CH(NCH}_3\text{)(CH}_2\text{)}_2\text{CHCH}_2\text{-}$  ;

R<sup>6</sup>/R<sup>7</sup> are H/OH; =O, or -S(CH<sub>2</sub>)<sub>2</sub>S-,

R<sup>8</sup> is H, COOR<sup>9</sup>, CONHR<sup>10</sup>, CSNHR<sup>11</sup>, COR<sup>12</sup>, SO<sub>2</sub>R<sup>13</sup>, lower alkyl, aryl lower alkyl, heteroaryl wherein the heteroatoms include 1 to 3 N atoms and the substituents are halo or amino, heteroaryl lower alkyl wherein heteroaryl is 6-membered and the heteroatoms are N, or aryl lower alkyl substituted with 1 substituent selected from lower alkyl, alkoxy, and halo;

R<sup>9</sup> is lower alkyl, aryl lower alkyl, aryl, tetrahydrofuranyl, tetrahydropyranyl, or aryl substituted by 1 to 2 substituents selected from lower alkyl, alkenyl, alkoxy, methylene dioxy, and halo;

R<sup>10</sup> and R<sup>11</sup> are each independently aryl, aryl lower alkyl, or aryl substituted by 1 substituent selected from lower alkyl, halo, alkoxy, trifluoromethyl, and pentafluoroethyl;

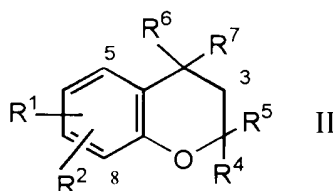
R<sup>12</sup> is lower alkyl, aryl, aryl lower alkyl, heteroaryl lower alkyl wherein the heteroatoms are N, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from S and N

lower alkyl, or aryl substituted with 1 substituent selected from lower alkyl, alkoxy, halo, sulfamoyl, cyano, or phenyl; and

$R^{13}$  is lower alkyl, aryl, or aryl substituted with 1 substituent selected from lower alkyl, alkoxy, and halo;

or a pharmaceutically acceptable salt thereof.

46. A compound of the formula:



wherein:

$R^1$  is  $O(CH_2)_{1-2}OH$ ,  $CO_2H$ ,  $O-Z-C(O)NH(CH_2)_{1-6}R^{17}$  or  $OCH_2-4-Phe-C(O)NH(CH_2)_{1-6}R^{17}$ ;

$R^2$  is H or lower alkyl;

$R^3$  is H, alkyl, aryl, or arylalkyl;


$R^4$  and  $R^5$  are each independently H, lower alkyl, or substituted lower alkyl where the substituents are 1-3 alkoxy, aryl, substituted aryl, carboalkoxy, carboxamido or di-loweralkylamido; or

$R^4$  and  $R^5$  taken together are  $-(CH_2)_n-$ ,  $-(CH_2)_2-O-(CH_2)_2-$ ,  $-CH_2-O-(CH_2)_3-$ ,  $-(CH_2)_2-NR^8-CH_2)_2-$ ,  $-CH_2-NR^8-(CH_2)_m-$ ,  $-(CH_2)_2CH(NHR^8)(CH_2)_2-$ ,  $-(CH_2)_2-S(O)_{0-2}-(CH_2)_2-$ , or  $CH_2CH(N-loweralkyl)(CH_2)_2CHCH_2-$ ;

one of  $R^6$  and  $R^7$  is H and the other is H, OH, or  $N(CH_2)_{1-6}R^{14}R^{15}$ ; or

$R^6$  and  $R^7$  taken together are , with the proviso that

when  $R^1$  is  $-OH$  and  $R^2$  is  $-H$ ,  $R^6$  and  $R^7$  are not  $-H$  and  $-OH$  or when taken together are

not  ;

- $R^8$  is H,  $\text{COOR}^9$ ,  $\text{CONHR}^{10}$ ,  $\text{CSNHR}^{11}$ ,  $\text{COR}^{12}$ ,  $\text{SO}_2\text{R}^{13}$ , lower alkyl, aryl lower alkyl, heteroaryl, or heteroaryl lower alkyl, wherein aryl is optionally substituted with 1-3 substituents selected from lower alkyl, lower alkoxy, halo, CN,  $\text{NH}_2$ ,  $\text{COOH}$ ,  $\text{CONH}_2$ , carboalkoxy, and mono- or di-lower alkylamino and wherein heteroaryl is a mono- or bicyclic heteroaromatic ring system of 5 to 10 members including 1 to 3 heteroatoms selected from O, N, and S and 0-3 substituents selected from halo, amino, cyano, lower alkyl, carboalkoxy,  $\text{CONH}_2$ , and S-lower alkyl;
- $R^9$  is lower alkyl, aryl, aryl lower alkyl, heteroaryl, aryl substituted by 1-3 substituents selected from alkyl, alkenyl, alkoxy, methylene dioxy, and halo, or a 5- to 6-membered heterocyclic ring containing O or N as a heteroatom, wherein heteroaryl is a heteroaromatic ring of 5 to 6 members including 1 to 2 heteroatoms selected from O, N, and S and 0-2 substituents selected from lower alkyl, dialkylamino, lower alkoxy, and halo;
- $R^{10}$  and  $R^{11}$  are each independently lower alkyl, aryl, aryl lower alkyl, or aryl substituted by 1-3 substituents selected from lower alkyl, halo, alkoxy and haloalkyl;
- $R^{12}$  is lower alkyl, aryl, heteroaryl, aryl lower alkyl, heteroaryl lower alkyl, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from O, S, and N, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from O, S, and N-lower alkyl, or aryl substituted with 1-3 substituents selected from lower alkyl, alkoxy, halo, sulfamoyl, lower alkyl sulfamoyl, cyano, and phenyl;
- $R^{13}$  is lower alkyl, aryl, or aryl substituted with 1-3 substituents selected from lower alkyl, alkoxy, halo, CN, and haloalkyl;
- $R^{14}$  is H; alkyl; alkyl substituted by 1-3 alkoxy, S-lower alkyl, sulfamoyl, halo, alkylsulphonamido, or arylsulphonamido; alkenyl; alkynyl; aryl; substituted aryl; heteroaryl; substituted heteroaryl; heterocycloalkyl;  $-\text{CH}_2\text{NR}^{16}\text{C}(\text{O})\text{R}^{16}$ ;  $-\text{C}(\text{O})\text{NR}^{16}\text{R}^{16}$ ;  $-\text{CH}_2\text{OC}(\text{O})\text{R}^{16}$ ; or  $-\text{CH}_2\text{SC}(\text{O})\text{R}^{16}$ ;

R<sup>15</sup> is H, alkyl, -C(O)X, -C(S)X, or -C(NCN)NR<sup>3</sup>R<sup>3</sup>;

R<sup>16</sup> is lower alkyl, substituted lower alkyl, aryl, or substituted aryl;

R<sup>17</sup> is H; alkyl, alkyl substituted by 1-3 alkoxy, S-lower alkyl, sulfamoyl, halo, alkylsulphonamido, or arylsulphonamido; alkenyl; alkynyl; aryl; substituted aryl; heteroaryl; substituted heteroaryl; heterocycloalkyl; -CH<sub>2</sub>NR<sup>16</sup>C(O)R<sup>16</sup>; -C(O)NR<sup>16</sup>R<sup>16</sup>; -CH<sub>2</sub>OC(O)R<sup>16</sup>, or -CH<sub>2</sub>SC(O)R<sup>16</sup>;

X is alkyl, aryl, arylalkyl, O-loweralkyl, or -NR<sup>3</sup>R<sup>3</sup>;

Z is -(CH<sub>2</sub>)<sub>1-6</sub>-, optionally substituted with 1-3 lower alkyl; -CHR<sup>2</sup>-; -Phe-CH<sub>2</sub>-, where Phe is optionally mono-substituted with halogen, lower alkyl, or alkoxy; or heteroarylene-(CH<sub>2</sub>)<sub>n</sub>;

m is 2 or 3; and

n is 4-9;

or a pharmaceutically acceptable salt thereof.

47. A compound of claim 46, wherein R<sup>12</sup> is sulfamoylphenyl.

48. A compound of claim 46, wherein R<sup>12</sup> is *p*-sulfamoylphenyl.

49. A compound of claim 46, wherein:

R<sup>1</sup> is OCH<sub>2</sub>C(O)NH(CH<sub>2</sub>)<sub>1-6</sub>R<sup>17</sup>, or OCH<sub>2</sub>-4-Phe-C(O)NH(CH<sub>2</sub>)<sub>1-6</sub>R<sup>17</sup>;

R<sup>4</sup> and R<sup>5</sup> are each lower alkyl; or

R<sup>4</sup> and R<sup>5</sup> taken together are -(CH<sub>2</sub>)<sub>5</sub>-, -(CH<sub>2</sub>)<sub>2</sub>-O-(CH<sub>2</sub>)<sub>2</sub>-, -(CH<sub>2</sub>)<sub>2</sub>-NR<sup>8</sup>-(CH<sub>2</sub>)<sub>2</sub>-,  
-(CH<sub>2</sub>)<sub>2</sub>-CH(NHR<sup>8</sup>)(CH<sub>2</sub>)<sub>2</sub>-, -(CH<sub>2</sub>)<sub>2</sub>-S-(CH<sub>2</sub>)<sub>2</sub>-, or CH<sub>2</sub>CH(NCH<sub>3</sub>)(CH<sub>2</sub>)<sub>2</sub>CHCH<sub>2</sub> ;

R<sup>6</sup>/R<sup>7</sup> are H/OH; =O, or -S(CH<sub>2</sub>)<sub>2</sub>S-;

R<sup>8</sup> is H, COOR<sup>9</sup>, CONHR<sup>10</sup>, CSNHR<sup>11</sup>, COR<sup>12</sup>, SO<sub>2</sub>R<sup>13</sup>, lower alkyl, aryl lower alkyl, heteroaryl wherein the heteroatoms include 1 to 3 N atoms and the substituents are halo or amino, heteroaryl lower alkyl wherein heteroaryl is 6-membered and the heteroatoms are

N, or aryl lower alkyl substituted with 1 substituent selected from lower alkyl, alkoxy, and halo;

R<sup>9</sup> is lower alkyl, aryl lower alkyl, aryl, tetrahydrofuranyl, tetrahydropyranyl, or aryl substituted by 1 to 2 substituents selected from lower alkyl, alkenyl, alkoxy, methylene dioxy, and halo;

R<sup>10</sup> and R<sup>11</sup> are each independently aryl, aryl lower alkyl, or aryl substituted by 1 substituent selected from lower alkyl, halo, alkoxy, trifluoromethyl, and pentafluoroethyl;

R<sup>12</sup> is lower alkyl, aryl, aryl lower alkyl, heteroaryl lower alkyl wherein the heteroatoms are N, a 5- or 6-membered heterocyclic ring containing 1-2 heteroatoms selected from S and N lower alkyl, or aryl substituted with 1 substituent selected from lower alkyl, alkoxy, halo, sulfamoyl, cyano, or phenyl; and

R<sup>13</sup> is lower alkyl, aryl, or aryl substituted with 1 substituent selected from lower alkyl, alkoxy, and halo;

or a pharmaceutically acceptable salt thereof.

### Remarks

### Status of Claims

1-37	Claims of priority application
1-3 and 15-37	Canceled by preliminary amendment
38	Added by July 24, 2000 amendment
8-14	Canceled without prejudice in this paper
39-49	Added in this paper
4-7 and 39-49	Pending following entry of this paper